



1623  
JFW

Appl. No. : 09/807,402  
Applicant : Hofert et al.  
Filed : August 3, 2001  
Title : COMBINATION OF GESTAGENS AND SUGARS  
TC/A.U. : 1623  
Examiner : L. C. Maier  
Docket No. : SCH-1808

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**SUPPLEMENTAL REPLY**

Sir:

Further to the Reply filed on September 27, 2004, attached is the declaration discussed therein.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

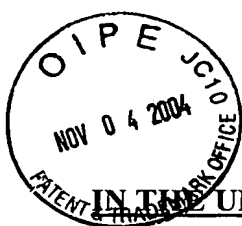
Respectfully submitted,

Csaba Henter, Reg. No. 50,908  
Anthony J. Zelano, Reg. No. 27,969  
Attorneys for Applicant(s)

MILLEN, WHITE, ZELANO  
& BRANIGAN, P.C.  
Arlington Courthouse Plaza 1, Suite 1400  
2200 Clarendon Boulevard  
Arlington, Virginia 22201  
Telephone: (703) 243-6333  
Facsimile: (703) 243-6410

Date: November 4, 2004

K:\Sch\1808\Reply (suppl) Nov 04.doc



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Appl. No. : 09/807,402  
Applicant : Hofert et al.  
Filed : August 3, 2001  
Title : COMBINATION OF GESTAGENS AND SUGARS  
TC/A.U. : 1623  
Examiner : L. C. Maier

**DECLARATION UNDER 37 C.F.R. §1.132**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

I, Thomas Backensfeld, being duly warned, declare that:

I am a listed inventor of the above-captioned application and am, therefore, familiar with the invention described therein and with the grounds for rejection made against the claims of the application in the Office Action mailed January 26, 2004, from the U.S. Patent and Trademark Office.

My expertise for making this declaration is demonstrated in the attached CV. If a patent issues from this application and if it is decided by the assignee to pursue a commercial product falling under its claims and if such a commercial product is approved by FDA and sold in the US, then under German law, I and the other inventors will receive some income derived from such sales.

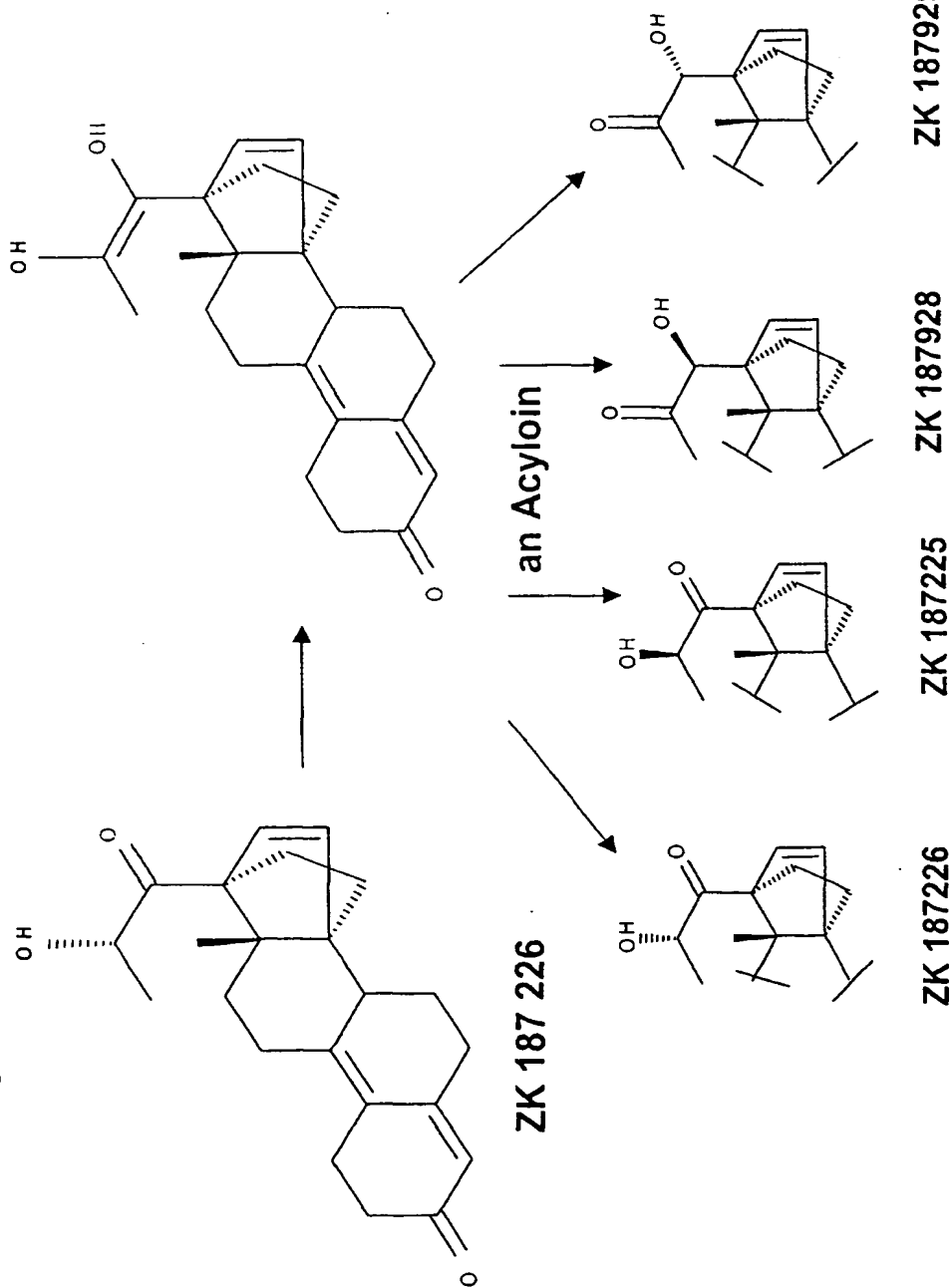
The following experiments were conducted by me or under my supervision.

Compounds of formula I of the claims are subject to acyloin rearrangement during storage, in which case variants occur as discussed in the specification of this application. ZK 187226 is a compound of the invention and has the chemical structure illustrated on page 2. (This compound is a tautomer existing in the (H, OH) or (=O) forms, as shown.) Page 2 also illustrates acyloin rearranged variants of the compound ZK 187226, identified as ZK 187225, ZK 187928 and ZK 187929.

Side-by-side storage stability comparative tests of tablets containing ZK 187226 are conducted without and with the presence of  $\beta$ -cyclodextrin in the tablets. The results are depicted in HPLC chromatograms on pages 3 and 4, respectively, and are identified as (Control) and ( $\beta$ -CD-Clathrate), respectively. The tablets were stored for 1,5 months under a variety of conditions identified on the chromatograms, i.e., -18°C; 25°C; 25°C, 60% r.h.; etc. (where "r.h." means relative humidity).

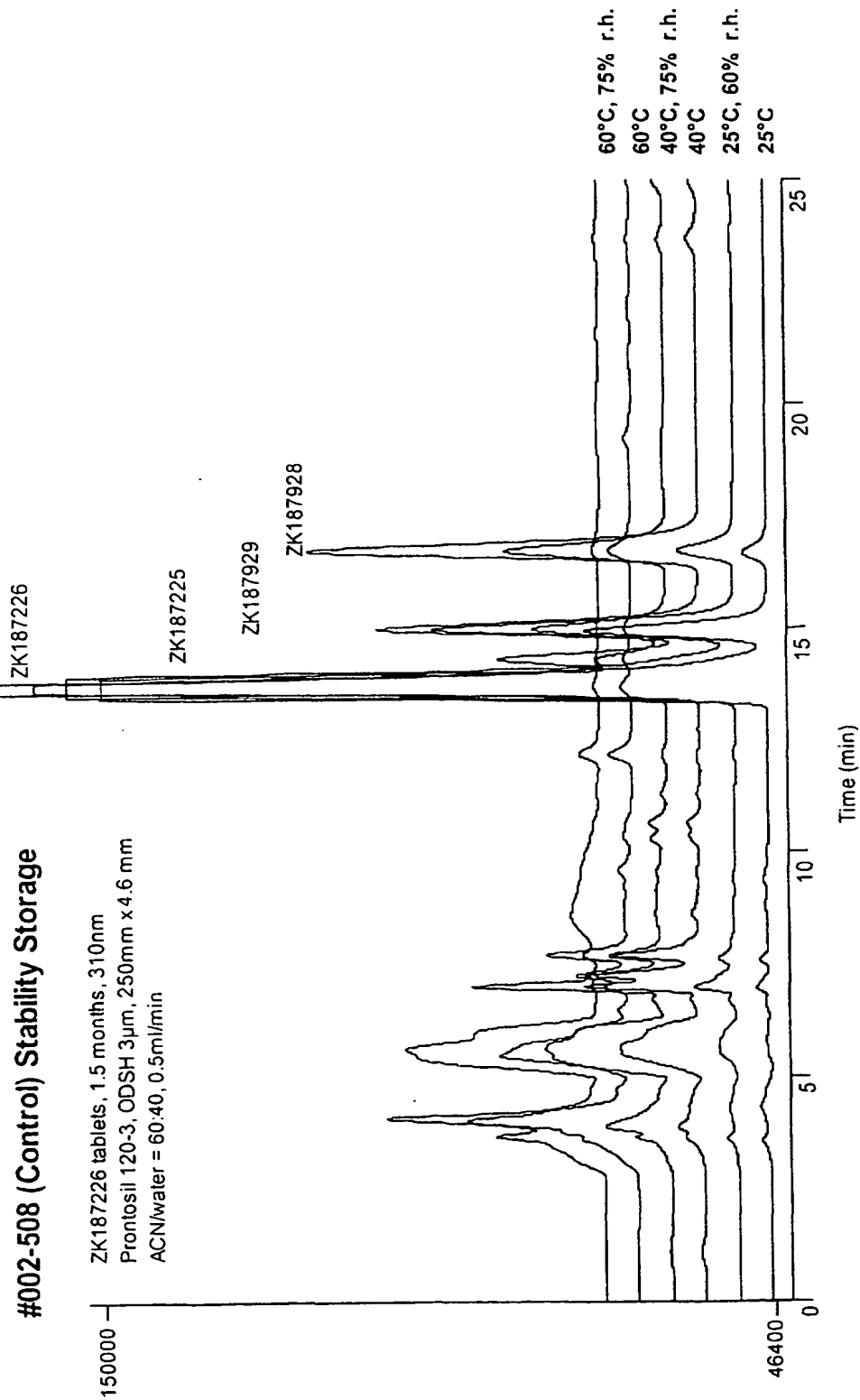
# Decomposition Pathway

## Decomposition Pathway: Acyloin Rearrangement



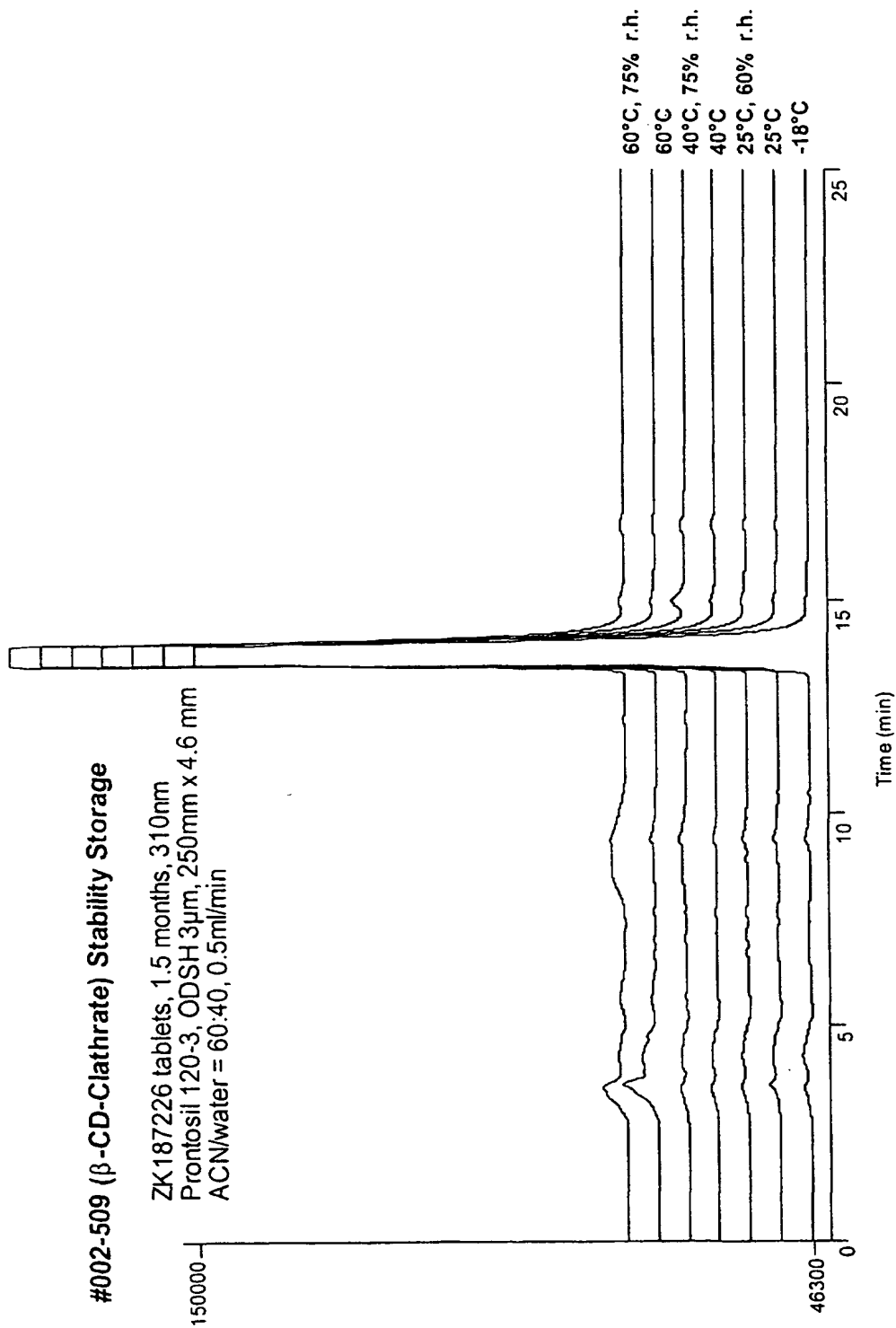
ZK 187 226

# HPLC Chromatogram



ZK 187226

# HPLC Chromatogram



ZK 187226

The chromatogram on page 3, where no  $\beta$ -cyclodextrin is present in the tablets, shows a number of peaks for compounds other than ZK 187226, including significant peaks for each of the acyloin rearranged variants of the compound ZK 187226, especially at higher temperatures and relative humidity.

The chromatogram on page 4, where  $\beta$ -cyclodextrin is present in the tablets, shows no significant peaks for compounds other than ZK 187226, meaning that acyloin rearrangement of ZK 187226 was prevented by the addition of  $\beta$ -cyclodextrin to the tablets.

The test results demonstrate that compounds of formula I in tablets according to the claims are significantly more stable than tablets that do not contain  $\beta$ -cyclodextrin and that  $\beta$ -cyclodextrin stabilized ZK 187226 from degradation through acyloin rearrangement, which was not expected from the prior art. Acyloin rearrangement represents a significant degradation mechanism as significant size peaks are present for the acyloin rearranged variants of ZK 187226. Accordingly, the results are significant and would not have been expected by those in this field from the disclosure of Backensfeld or otherwise.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

 10/25/2004

Thomas Backensfeld

Date

## **Curriculum Vitae**

### **Dr. Thomas Backensfeld**

---

#### **Personal**

Name: Dr. Thomas Backensfeld  
Place of residence: D - 13127 Berlin  
Date of birth: 22.12.1959  
Marital Status: married, 2 children  
Nationality: German  
High School: 1979  
Military Service: 1979 - 1980  
Occupation: Pharmacist  
Language: German, English  
(French and Japanese basics)

#### **Professional**

1980 - 1984: University of Münster, Germany - Study of Pharmaceutical Sciences  
1985: Practical education in pharmacy (public pharmacy; hospital pharmacy)  
1986 - 1990: University of Kiel, Germany - PhD thesis in Pharmaceutics and training of students  
1990, Nov. 01: Schering AG, Berlin  
1990 - 1992: Head of analytical working group in 'Pharma Labor' department: Analytics of all kind of dosage forms  
1992 - 2001: Head of formulation working group in 'Oral Dosage Formulation' department: Preformulation, Formulation and Manufacturing of all kind of oral dosage forms  
1996: Pharmacuetical Development - group leader in formulation development group  
2001: Head of formulation development group in 'Oral Dosage Formulation' department  
2002: Head of 'Production of Highly Potent Drugs / Bulk Weighing' department: Plant manager